CONSTITUTION AND COLOR
IN THE
THIOFLAVINE GROUP

DISSERTATION

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CONSTITUTION AND COLOR IN THE THIOFLAVINE GROUP

I. Purpose of the Investigation.

This investigation was undertaken to develop additional evidence for the constitution of Thioflavine T, with special reference to the position of the methyl halide group and the effect of its position on color; and to study the effect of constitution on the color of dyes in this series.

II. Method of Attack.

(1). An attempt was made to prepare 2 (p-aminophenyl) benzothiazole, 6-dimethylamino-2(p-aminophenyl)benzothiazole, 6-amino-2(p-aminophenyl) benzothiazole and 2-2′ di(p-aminophenyl) benzobisthiazole, and to methylate these compounds with methyl alcohol and hydrochloric acid to produce dyes of the Thioflavine type.

(2). 2(p-Dimethylaminophenyl) benzo-and substituted benzothiazoles were prepared by the action of p-dimethylaminobenzaldehyde on:

- (a) o-Aminophenyl-disulfide or its zinc salt.
- (b) 2-Amino-5-dimethylaniline-thiosulfuric acid.
- (c) p-Phenylenediamine-monothiosulfuric acid.
- (d) The potassium salt of the 1-4-dithiosulfuric acid derivative of p-phenylenediamine.

The products formed by the above reaction were treated with methyl iodide.

(3). p-Dimethylamino-benzaldehyde was treated with methyl iodide and the quaternary salt thus formed was condensed with the series of compounds listed under (2).

III. Results and Conclusions.

(1). The method of preparation of 6-dimethylamino-2-phenyl-benzothiazole was improved by using dilute alcohol as the condensing medium. The yield was increased from 10 to 50 percent.

(2). Thiazoles were prepared by the action of acid chlorides on o-amino-thiosulfuric acid derivatives. This is contradictory to a statement of Heller and co-workers that thiazoles could not be prepared by this method.

(3). 6-Amino-2-phenyl-benzothiazole was prepared by a direct method which definitely establishes the position of the amino group. This compound is identical with that prepared by Bogert and Abrahamson[21] from 2-phenyl-benzothiazole by nitration and subsequent reduction, thus substantiating their conclusions as to the position of entry of the nitro group, and also confirming the proof obtained by Bogert and Corbitt.[28]

(4). A quaternary salt of 6-dimethylamino-2-phenyl-benzothiazole was prepared by the action of methyl iodide on 6-dimethylamino-2-phenyl-benzothiazole. Previous investigators[21] failed to obtain a quaternary salt by methylation of the corresponding 6-amino derivative.

(5). Several new anils of the type previously reported by Bogert and Updike[29] were isolated. A new method of cyclizing these anils to produce thiazoles was discovered. The results of this process furnish additional evidence for the mechanism of the reaction involved in the formation of thiazoles from o-amino-thiosulfuric acid derivatives.

(6). A new process was perfected for the preparation of Thioflavine dyes by the action of methyl iodide on dimethylamino-thiazoles. This process yields products that can be readily purified. Several interesting isomeric compounds were obtained, also a dimethiodide.

(7). A method for the preparation of the methiodide of p-dimethylamino-benzaldehyde in almost quantitative yields was developed.

(8). The use of p-iodo-trimethylamino-benzaldehyde for the preparation of isomeric Thioflavine types produced some interesting new products.

(9). Substantial evidence for the formula of Thioflavine T, proposed by Green[7, 8] has been developed.

(10). Several new homologues of Thioflavine T were prepared and dye tests were performed.

(11). The following new compounds were prepared during the course of the investigation.

1. 2-(p-dimethylaminophenyl) benzothiazole. (a)* 7.
2. 2(p-iodotrimethylaminophenyl) benzothiazole. (b) 9.
3. 2(p-Dimethylaminophenyl) benzothiazole 3-methiodide. (c)* 8.
4. 2-Phenyl-6-dimethylamino-benzothiazole - (monomethiodide) ? (d) 14.
5. 2(p-Iodotrimethylaminophenyl) - 6 - dimethylamino-benzothiazole. (e) 17.
6. 2(p-Dimethylaminophenyl)-6-dimethylamino - benzothiazole-(monomethiodide) ? (f) 16.
7. 2(p-Dimethylaminophenyl)-6-dimethylamino - benzothiazole-(dimethiodide) ? (g) 16.
8. 2(p-Nitrophenyl)-6(p-nitrobenzoylamino) - benzothiazole. (h) 20.
9. 2(p-Nitrophenyl)-6-amino-benzothiazole. (i) 21.
10. 2(p-Aminophenyl)-6-amino-benzothiazole. (j) 22.
11. 2(p-Dimethylaminobenzal)-5-amino - aniline - thiosulfuric acid. (k) 23.
12. 2(p-Dimethylaminophenyl)-6-amino-benzothiazole. (l) 23.
13. 2(p-Nitrophenyl)-6(p-nitrobenzalamino) - benzothiazole. (m) 24.
14. 2(p-Iodotrimethylaminophenyl) - 6(p-iodotrimethylaminophenyl)-benzalamino)-benzothiazole. (n) 25.
15. 2(p-Dimethylaminophenyl) - 6(p-dimethylamino-benzalamino)-benzothiazole-5-thiosulfuric acid. (o) 28.
16. 2-2′-Di(p-dimethylaminophenyl)-benzobisthiazole. (p) 28.

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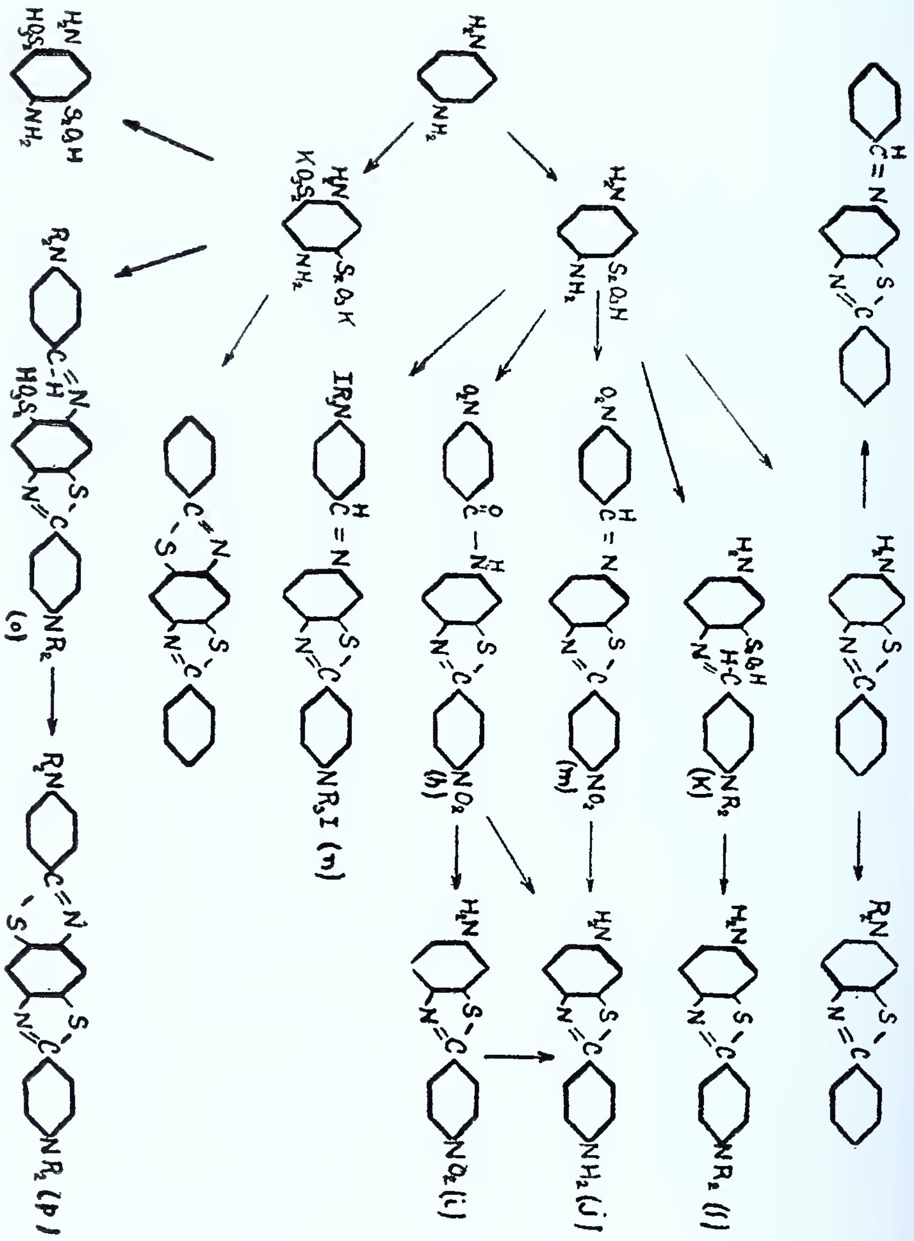
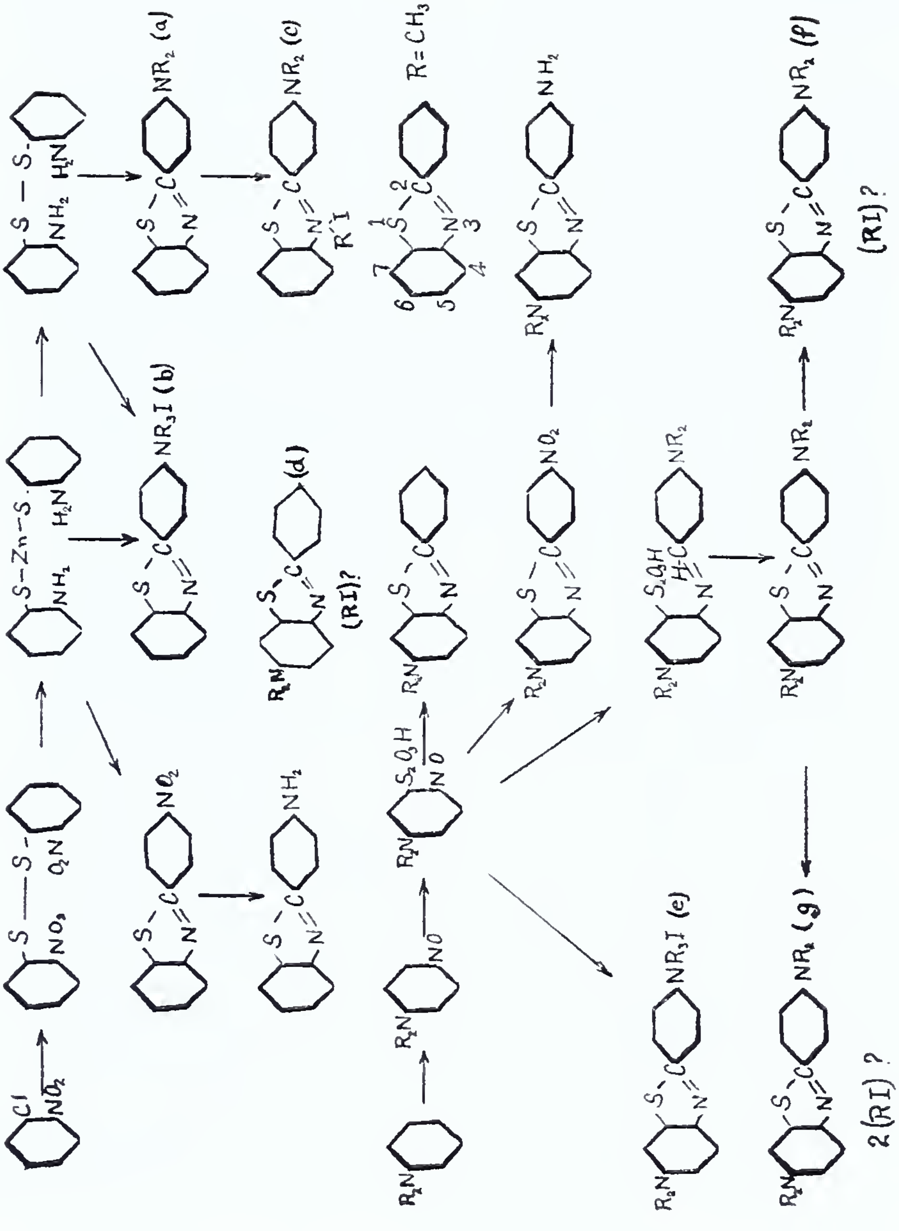
* (Small letters) refer to flo sheet. Numbers refer to experiments under Experimental.


(h)
(i)
(j)
(K)
(l)
(m)
(n)
(o)
(p)
NO₂
NH₂
NR₂
NR₃I
R₂N
H₂N
O₂N
S₂O₃H
S₂O₃K
HO₃S
KO₃S


NR₂ (a)
NR₃I (b)
NR₂ (c)
R'I
(d)
(RI)?
R=CH₃
1 2 3 4 5 6 7
NR₃I (e)
NR₂ (f)
(RI)?
NR₂ (g)
2(RI)?
S₂O₃H
NO
NO₂
NH₂
S—Zn—S
Cl
R₂N

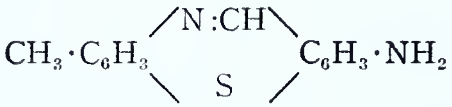
NOMENCLATURE

The system of nomenclature used in this investigation is in agreement with previous publications on benzothiazoles from this laboratory.[21, 25, 28, 29, 31]

HISTORICAL AND DISCUSSION

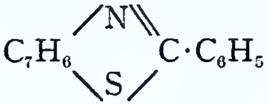
Dehydrothio-p-toluidine is probably the most valuable intermediate used in the manufacture of thiazole dyestuffs. The first record of its preparation is in a German patent of 1885,[4] but at that time, it was believed to be an isomer of thio-p-toluidine which had been prepared by Merz and Weith.[1, 2] The former was prepared by heating one mole of sulfur with two moles of p-toluidine for 24 hrs. at 175-185° C.

Two years later Green fused 2-3 moles of sulfur with two moles of p-toluidine at 175° C. and from the melt isolated dehydrothio-p-toluidine and primuline. In 1888[5] he published an article introducing a new class of dyes including Primuline as a direct dye and as a base for related ingrain dyes. He failed to mention however, the method of preparing primuline and during the same year British patents appeared covering the preparation of thiobases by sulfur fusion. Green[7, 8] did not publish his article covering the preparation of dehydrothio-p-toluidine and primuline until 1889. In this article he proposed the following formula for dehydrothio-p-toluidine:

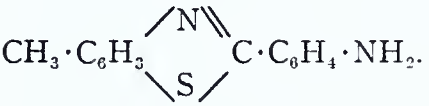


$$CH_3\cdot C_6H_3\begin{matrix}\diagup N:CH\diagdown\\ \diagdown\quad S\quad\diagup\end{matrix}C_6H_3\cdot NH_2$$

Jacobson[11] in 1889 prepared and isolated pure dehydrothio-p-toluidine. Later in the same year Gatterman[12, 13] prepared and isolated the pure dehydro base and proved that it contained four atoms of hydrogen less than Merz and Weith's thiotoluidine. Gatterman[12, 13] also removed an amino group by boiling an alcoholic solution of the compound with nitrous acid and obtained the 2-phenyl derivative. Hess[3] had previously prepared this compound from 4-amino-thio-cresol and benzoyl chloride and formulated it as

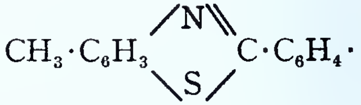


$$C_7H_6\begin{matrix}\diagup N\diagdown\!\!\diagdown\\ \diagdown S\diagup\end{matrix}C\cdot C_6H_5$$

Pfitzinger and Gatterman[14] also prepared 6-methyl-2-phenylbenzothiazole by oxidizing thiobenzotoluidine with potassium ferricyanide. Amino-thiocresol and benzoic acid were isolated as the degradation products from a potassium hydroxide fusion of the above 2-phenyl derivative. Dehydrothio-p-toluidine under similar treatment yielded amino - thiocresol and amino - benzoic acid. On the basis of these experiments, they proposed the now accepted formula for dehydrothio - p - toluidine  $CH_3\cdot C_6H_3\overset{\diagup N \diagdown\!\diagdown}{\underset{\diagdown S \diagup}{\qquad}}C\cdot C_6H_4\cdot NH_2$. Further evidence of this structure was obtained by Gatterman and Neuberg.[16] They synthesized p-nitro-thiobenzoyl-p-toluidine, oxidized it with potassium ferricyanide to 6-methyl-2(p-nitrophenyl) benzothiazole and upon reducing the nitro group obtained dehydrothio-p-toluidine.

The initial sulfur fusion method is the commercial process in use today. Attempts to control the reaction in order to produce exclusively either the dehydro or the primuline base, by varying the proportions and temperature, and using naphthalene as a diluent have failed. There are three different types of dyes prepared from the products of the sulfur fusion: (1) Primuline and related Ingrain dyes; (2) Columbia Yellow; and (3) Thioflavine dyes. The latter two are prepared from dehydrothio-p-toluidine. When only (1) and (2) are desired separation can be effected by sulfonating and taking advantage of the difference in solubility of the ammonium salts of the resulting sulfonic acids. When pure dehydro base is desired for the manufacture of Thioflavine T, separation must be effected by means of vacuum distillation or extraction with acids.

Since recent work on thiazole dyes has been largely devoted to Columbia Yellow types it seemed of major importance to bring the investigations in the Thioflavine types on a par with this work. Thioflavine T was first prepared by Green[7, 8] in 1889 and simultaneously by Rosenhek,[9, 10] by heating dehydrothio-p-toluidine with methyl alcohol and hydrochloric acid for 12 hrs. at 160-170° C. Without stating any reasons Green concluded that the quaternary salt formation took place on the cyclic nitrogen. G. Schultz[22] classifies the dye as the HCl salt, with the

CH_3Cl on the cyclic nitrogen and the HCl on the NR_2 group. Cain and Thorpe[23] classify the dye as  $CH_3\cdot C_6H_3\begin{matrix}/N\backslash\backslash\\ \backslash S/\end{matrix}C\cdot C_6H_4\cdot$ $N(CH_3)_3Cl$. Möhlau and Bucherer[20] place the methochloride on the sulfur as a sulfonium compound. In no case has any experimental evidence been offered for the conclusions as to the position of the methohalide group.

Bogert and Allen[28] in 1926 studied the effect of constitution and color in isomeric forms of Thioflavine T, by varying the position of the methyl group in the benzene nucleus and the amino group in the 2-phenyl nucleus. No evidence however, was obtained to show nitrogen formed the quaternary halide.

This investigation was undertaken to obtain further information concerning the effect of constitution on color, and to throw some light on the position of entry of the methohalide group and the effect of the position of this group on color. The original method of attack involved the preparation of the following thiazoles:

I. 2(p-aminophenyl) benzothiazole;
II. 6-dimethylamino-2-(p-aminophenyl) benzothiazole;
III. 6-amino-2(p-aminophenyl) benzothiazole; and
IV. 2-2′-di(p-aminophenyl) benzobisthiazole. By methylation of the above four compounds the corresponding series of Thioflavine T type dyes was expected.

Bogert and Snell[25] had previously prepared 2(p-aminophenyl) benzothiazole (I) from o-nitrochlorbenzene by the following series of reactions. o-Nitrophenyl disulfide was obtained by the action of alcoholic sodium disulfide on o-nitrochlorbenzene; reduction with zinc in glacial acetic acid produced the zinc salt of o-aminophenyl disulfide. The action of p-nitrobenzoyl chloride on the zinc salt with subsequent reduction of the nitro group gave the desired 2(p-aminophenyl)-benzothiazole.

6-Dimethylamino-2(p-aminophenyl) benzothiazole (II) was prepared according to the method of Bogert and Updike[29] with a few modifications. Starting with dimethylaniline, its p-nitroso hydrochloride was prepared, which was converted by the action of sodium thiosulfate in acetic acid into 2-amino-5-dimethylaniline-thiosulfuric acid. This compound was condensed with benzaldehyde, yielding 6-dimethylamino-2-phenyl - benzothiazole, m.p. 134-5° C. as reported. By carrying the reaction out in dilute alcoholic solution instead of glacial acetic acid, the yield was increased from 10% as previously reported to 50%. Heller, Quast and Blanc[26] stated that acid chlorides would not react with o-amino-thiosulfuric acid compounds to form thiazoles, but in the investigation 6-dimethylamino-2(p-nitrophenyl) benzothiazole was prepared by adding p-nitrobenzoyl chloride to a suspension of 2 - amino - 5 - dimethylaniline-thiosulfuric acid in glacial acetic acid. The nitro group was reduced with tin and hydrochloric acid and the corresponding 2(p-aminophenyl)-6-dimethylamino-benzothiazole was obtained.

6-Amino-2(p-aminophenyl) benzothiazole (III), was prepared from three different compounds. The preparation and purification of the intermediates was accomplished with considerable difficulty but resulted in the formation of several interesting new compounds.

p-Phenylenediamine-thiosulfuric acid was prepared by a modification of Bernthsen's[15] method. Since this compound has no melting point, for purposes of identification, it was condensed with benzaldehyde, hoping to obtain 6-amino-2-phenyl-benzothiazole. This thiazole had been previously prepared by Bogert and Abrahamson[21] from 2-phenyl-benzothiazole by nitration and subsequent reduction. Two products were obtained from the condensation, a white insoluble powder and a yellow crystalline product melting sharply at 168-169° C. (corr.). Failing to obtain the desired product, a sample of the thio acid was purified and analyzed. The results obtained from the analysis checked for the thio acid plus one mole of water of crystallization which was later proven to be present. Since excess benzaldehyde had been used in the previous condensation, the possibility of forming the 6-benzal derivative was considered. Bogert and Abrahamson had prepared this compound and reported a melting point of 151° C. Sulfur analysis of the new compound checked for the benzal derivative, so the work of Bogert and Abrahamson was repeated and their results verified. Prolonged boiling of the new compound in 40% sulfuric acid produced no change, whereas the real benzal derivative hydrolyzes very readily in warm dilute acids. Sulfur fusion converts the compound melting 168-9° C. into 2-2′-diphenyl-benzobisthiazole, (a mixed melting point with a sample prepared from the dithio acid as described by Green[19] was unchanged). Carbon and hydrogen analysis indicated the possibility of a mercaptid or a disulfide. Insolubility in alkali seems to preclude the former, and molecular weight determinations failed to check for the latter. Since this compound did not seem to be directly related to the desired products, its further investigation was deferred. The white powder that was obtained from the condensation was boiled with hydrochloric acid. It dissolved and upon pouring into an excess of ammonium hydroxide a white precipitate separated. On purification this proved, by a mixed melting point, to be 6-amino-2-phenyl-benzothiazole. This is a direct proof of the position of the amino group in the compound prepared by Bogert and Abrahamson[21] from 2-phenylbenzothiazole by nitration and subsequent reduction. Methylation with methyl alcohol and hydrochloric acid yielded the dimethyl derivative reported by Bogert and Abrahamson[21] and a mixed melting point with 6-dimethylamino-2-phenyl-benzothiazole, prepared according to the directions of Bogert and Updike[29] was unchanged.

When p-phenylenediamine-monothiosulfuric acid was treated with p-nitrobenzoyl chloride a small amount of an orange colored product was obtained. Analytical results of this product corresponded to 6(p-nitrobenzoylamino)-2(p-nitrophenyl) benzothiazole. Hydrolysis with 40% sulfuric acid yields 6-amino-2(p-nitrophenyl) benzothiazole and reduction of either of the above compounds with tin and hydrochloric acid yields 6-amino-2(p-aminophenyl) benzothiazole.

When p-nitrobenzaldehyde is substituted for the acid chloride in the above reaction 6(p-nitrobenzalamino)-2(p-nitrophenyl) benzothiazole is obtained. This compound is analogous to that prepared by Bogert and Sevag[31] in the toluene series and like it, resists all attempts to hydrolyze to the 6-amino derivative. Reduction with tin and hydrochloric acid produces 6-amino-2(p-aminophenyl) benzothiazole and a mixed melting point with the same compound prepared from the above p-nitrobenzoyl derivative was unchanged.

Attempts to prepare 2-2′-di(p-nitrophenyl) benzobisthiazole (IV) and the corresponding amino derivative were unsuccessful.

Methylation of these three amines with methyl alcohol and hydrochloric acid gave products that, even after numerous purifications, failed to yield satisfactory analytical results so the method of attack was varied as follows: p-Dimethylamino-benzaldehyde was substituted for p-nitrobenzaldehyde and p-nitrobenzoyl-chloride, and the resulting 2-(p-dimethylaminophenyl) thiazoles were heated in a Parr bomb with excess methyl iodide for 12 hrs. at 100-110° C. This method resulted in the formation of the quaternary salts without the formation of any halogen acid and the products so obtained were readily purified for analysis.

The quaternary methiodide obtained from 2(p-dimethylaminophenyl) benzothiazole was fairly soluble in hot water from which it crystallized on cooling in light yellow plate-like crystals. An isomeric compound was obtained by the action of methyl iodide on 6-dimethylamino-2-phenyl-benzothiazole. This methiodide crystallized from water in almost colorless mica-like plates.

6- Dimethylamino-2(p-dimethylaminophenyl) benzothiazole reacted with methyl iodide to form two quaternary salts; one a reddish orange mono methiodide, moderately soluble in water and extremely soluble in alcohol and the other a dimethiodide, extremely soluble in water and only moderately soluble in alcohol. The dimethiodide was light yellow in color and its solution was practically colorless except for a slight greenish fluorescence which is characteristic of the solutions of the 2-amino-phenyl and the 2-dimethylaminophenyl-benzothiazoles.

6-Amino-2(p-dimethylaminophenyl) benzothiazole was not treated with methyl iodide, because, if the reaction proceeded normally, it could only result in the production of the methiodide prepared from the corresponding 6-dimethylamino derivative.

The action of methyl iodide on 2-2′-di(p-dimethylaminophenyl) benzobisthiazole was unsatisfactory. Increase in weight during methylation corresponded roughly to the addition of two moles of methyl iodide but no products could be isolated that contained even one atom of iodine per molecule. A decided decrease in the solubility of the product in alcohol occurred between successive recrystallizations, indicating the possibility that chemical reaction was taking place. The products were slightly soluble in hot water but on cooling always set to a thick gelatinous mass that could not be filtered. A fifty percent alcoholic solution appeared to be the best solvent.

Anils and a New Method of Cyclization to Produce Thiazoles.

Bogert and Updike[29] reported the formation of an anil as an intermediate product in the preparation of 6-dimethylamino-2(p-dimethylaminophenyl) benzothiazole by the action of p-dimethylamino - benzaldehyde on 2-amino-5-dimethylaniline-thiosulfuric acid. They carried the reaction out in acetic acid and obtained a mixture of the anil and the thiazole, the former being converted into the thiazole by prolonged boiling in glacial acetic acid. By carrying the reaction out in 50% alcoholic solution the anil was precipitated in small glistening red needles and no thiazole was isolated. In the other two analogous cases met with in this investigation, a similar reaction seemed to occur and red crystalline precipitates were obtained. The anil formed from the potassium salt of p-phenylenediamine-dithiosulfuric acid was purified and analyzed. Results from a sulfur analysis failed to check for the bis anil type expected but indicated that ring closure had been effected on one side. This was further substantiated by proving the presence of approximately one mole of sulfurous acid in the filtrate per mole of product isolated. This was accomplished by heating the filtrate up with a little nitric acid and precipitating the sulfuric acid formed with barium chloride. Attempts to effect further ring closure by boiling the anil in glacial acetic acid failed. When heated in nitrobenzene a decided odor of sulfur dioxide was observed but no satisfactory separation of thiazole was accomplished. When heated with aniline a reaction occurred at a relatively low temperature and the mixture turned to a thick paste that became more fluid as the aniline began to boil. On filtering the boiling mixture a white residue was left in the funnel and a yellow crystalline product separated as the filtrate cooled. The yellow product proved to be the desired 2-2′-di(p-dimethylaminophenyl) benzobisthiazole. This same procedure was applied to the other anils with similar results thus saving the prolonged boiling in glacial acetic acid. Some of the white residue was tested and appears to be a sulfite salt of aniline. The intermediate product formed in the warm aniline was filtered off but attempts to purify it were unsuccessful. It was thought that the aniline probably added to the thiosulfuric acid radical forming a salt and then instead of splitting off sulfurous acid, as was postulated by Bogert and Updike in their reaction, split off the aniline salt.

The use of p-dimethylamino-benzaldehyde gave a clue to a possible method of determining the position of entry of the methohalide group. If the above aldehyde would react with methyl iodide to form a quaternary salt and the thiazole could be prepared from this new aldehyde, then the position of the methiodide would be established and the products formed could be compared with those prepared by the other methods. If the compounds were identical then Cain and Thorpe's[23] formula would be correct; if different then Green[7, 8] or possibly Möhlau and Bucherer's[20] would be correct. Hodgson and Cooper[30] prepared the methiodide by refluxing p-dimethylamino-benzaldehyde with methyl iodide but failed to report yields. By heating the two in a Parr bomb for 6 hrs. at 90-100° C. an almost quantitative yield was obtained. This quaternary salt of the aldehyde was condensed with the zinc salt of o-aminophenyl-disulfide and the o-amino-thiosulfuric acid derivatives previously mentioned.

2-(p-iodo trimethylaminophenyl) benzothiazole was obtained by the above reaction with the zinc salt. The product was moderately soluble in hot water from which it crystallized in almost clear mica-like plates.

2-Amino-5-dimethylaniline-thiosulfuric acid reacted with the quaternary salt of the aldehyde producing a brown crystalline compound which was moderately soluble in water.

When p-phenylenediamine-monothiosulfuric acid was condensed with the above aldehyde a white product was obtained. This compound was exceedingly soluble in water and only slightly soluble in alcohol. Analysis indicated that two moles of the quaternary salt had reacted with one of the thio acid to form the p-iodotrimethylaminobenzal derivative of 6-amino-2(p-iodotrimethylaminophenyl) benzothiazole.

Attempts to prepare a dimethiodide of a similar type from the potassium salt of the 1-4-dithiosulfuric acid derivative of p-phenylenediamine were unsuccessful. The hydrochloric acid required to produce the free dithio acid appeared to effect the reaction and the odor of hydrogen sulfide was detected.

Since the methiodides obtained by this last method do not correspond to those prepared by the methylation of 2(p-dimethylaminophenyl) benzothiazole the formula postulated by Cain and Thorpe[23] appears to be erroneous. Mills, Clark and Aeschlimann[24] treated the methiodide of benzothiazole with strong sodium hydroxide and obtained o-methylaminophenyl-disulfide. Later Clark [27] extended this work to the 2-phenyl derivatives and succeeded in isolating o-methylbenzoylaminomercaptide. These experiments prove that Möhlau and Bucherer's[20] assumption of a sulphonium type is very improbable, therefore Green's[7, 8] formula appears to be correct.

Dye Tests

Dye tests were carried out on all the methiodides using a purified sample of commercial Thioflavine T as a standard. The methiodides prepared by the action of methyl iodide on the dimethylamino-thiazoles gave the following tests on silk, (see p. 34).

(1) Methiodide of 6-dimethylamino-2-phenylbenzothiazole. The solution was colorless and no perceptible color was produced on the fiber.

(2) Methiodide of 2(p-dimethylaminophenyl) benzothiazole. The solution was light yellow and dyed silk a light yellow slightly lighter than the standard.

(3) The monomethiodide of 6-dimethylamino-2(p-dimethylaminophenyl) benzothiazole. The solution of this dye was orange and dyed silk a brilliant yellow decidedly more vivid than the standard but the greenish undertone was not as pronounced.

(4) The dimethiodide of 6-dimethylamino-2 (p-dimethylaminophenyl) benzothiazole. The solution of this compound was colorless and no perceptible color was imparted to the fiber.

The methiodides prepared by the action of benzaldehyde-p-trimethylammonium iodide were also dye tested with the following results.

(1) 2(p-Iodotrimethylaminophenyl) benzothiazole. The solution of this quaternary salt is colorless and imparts no perceptible color to silk.

(2) 6-Dimethylamino-2(p-iodotrimethylaminophenyl) benzothiazole. The solution of this compound is very light yellow with a decided greenish fluoresence and produces a similar effect on silk.

(3) The p-iodotrimethylaminobenzal derivative of 6-amino-2(p-iodotrimethylaminophenyl) benzothiazole. This compound is very soluble in water to which it imparts a greenish fluorescence. It imparts a very light greenish color to silk.

EXPERIMENTAL

1. o-Nitrophenyl-disulfide.

This compound was prepared from o-nitrochlorbenzene by the method described by Wohlfahrt.[18] Thirty-two grams of o-nitrochlorbenzene were dissolved in 50 cc. of alcohol and refluxed with an alcoholic solution of sodium disulfide, made by heating 36 g. of sodium sulfide with 4.8 g. of sulfur in 150 cc. of alcohol. After refluxing two hrs. the mixture was allowed to cool. It was then filtered, washed with water and then alcohol: yield 75% and m.p. 195° C. (corr.) were as reported.

2. o-Aminophenyl-disulfide, zinc salt.

This compound was prepared by the method of Bogert and Snell.[25] To a solution of 3.1 g. of o-nitrophenyl disulfide in 350 cc. of warm glacial acetic acid, zinc dust was added in small amounts until the yellow color disappeared. The hot solution was then filtered into two volumes of water. The zinc salt, which separated as a fine white precipitate, was filtered, washed and dried; yield 2.5 g. 81%.

3. o-Aminophenyl-disulfide.

This compound was prepared by the method of Bogert and Snell.[25] Air was drawn through a suspension of 3.2 g. of the zinc salt in a mixture of equal parts of water and concentrated ammonium hydroxide. After two hours the fine zinc salt was replaced by a crystalline precipitate of the disulfide. The precipitate was filtered and recrystallized from 25% alcohol. On cooling 1.3 g., 53% of yellow plate like crystals separated; m.p. 93° C. (corr.) agrees with that previously reported.

4. 2(p-Nitrophenyl) benzothiazole.

One gram of o-aminophenyl-disulfide, zinc salt, was suspended in 50 cc. of glacial acetic acid, heated to boiling and 1.2 g. of p-nitrobenzoyl-chloride were added. The zinc salt disappeared and after a few minutes a thick curdy precipitate separated. The mixture was kept warm for an hour, poured into four volumes of water and filtered; yield 1.5 g. 93%; m.p. after several recrystallizations from alcohol, 231-2° C. (corr.) agrees with that previously reported.

5. 2(p-Aminophenyl) benzothiazole.

This compound was prepared by the reduction of 2(p-nitrophenyl) benzothiazole as outlined by Bogert and Snell.[25] Two and a half grams of the nitro compound were suspended in 95 cc. of water and 5 cc. of conc. HCl and 10 g. of tin were added. The solution was boiled until the nitro compound disappeared. The solution was then poured into an excess of 4N. sodium hydroxide, heated for an hour, and filtered. The free base was recrystallized from alcohol; yield 1.5 g. 70%; m.p. of a purified sample 155° C. (corr.) checks that previously reported.

6. Methylation of 2(p-aminophenyl) benzothiazole.

Two and three-tenth grams of 2(p-aminophenyl) benzothiazole, 3 g. of methyl alcohol and 1 g. of conc. HCl were heated in a sealed tube for 10 hours at 160-170° C. The contents of the tube were extracted with boiling water, filtered and the filtrate saturated with salt. A finely divided brown solid separated and was filtered off. After the product had been reprecipitated several times by salting out it was washed with alcohol, dried and analyzed. The discrepancy in analytical data is probably due to the presence of salt.

Analysis: Calc. for $C_{16}H_{18}N_2S\,Cl'_2$: S, 9.43
Found: S, 7.8

7. 2(p-Dimethylamino-phenyl) benzothiazole.

Five grams of o-aminophenyl)-disulfide were mixed with 3 g. of p-dimethylaminobenzaldehyde and the mixture was heated in an oil bath for 1 hour at 160-170° C. A vigorous reaction started around 150° C. After an hour the mass was poured into alcohol from which it was recrystallized. Three and four-tenth grams, 70% of white needle like crystals were obtained; m.p. 174-175° C. (corr.).

Analysis: Calc. for $C_{15}H_{14}N_2S$: C, 70.81; H, 5.55; S, 12.61
Found: C, 71.13; H, 5.28; S, 12.70

8. Methylation of 2(p-dimethylaminophenyl) benzothiazole.

Three grams of 2(p-dimethylaminophenyl) benzothiazole were heated in a Parr bomb with 5 cc. of methyl iodide for 12 hours at 100-110° C. The bomb was cooled, opened and after the excess methyl iodide had evaporated the yellow crystalline mass was extracted with hot water and the solution filtered. A slight residue of impurities was left and as the filtrate cooled the methiodide crystallized out in glistening yellow plates. Three and four-tenth grams, about 73% of crude crystals were obtained. The crude product was recrystallized several times from water and twice from methyl alcohol. When a sample was heated at the rate of 3° per min. it melted with decomposition at 223-4° C. (corr.) when placed in the bath at 215° C.

Analysis: Calc. for $C_{16}H_{17}N_2SI$: C, 48.46; H, 4.33
Found: C, 48.64; H, 4.29

9. 2(p-Iodo trimethylaminophenyl) benzothiazole.

One gram of zinc salt of o-aminophenyl-disulfide was suspended in 50 cc. of warm alcohol and HCl added until the zinc salt just dissolved. This solution was poured into a warm solution of 2 g. of the methiodide of p-dimethylamino-benzaldehyde dissolved in 50 cc. of alcohol. The solution was kept on a steam plate for 30 min. and allowed to cool. The product crystallized as the solution cooled in almost clear mica like crystals; yield 1.9 g. about 80%. After several recrystallizations from water the product melts with decomposition at 202-3° C. (corr.) when placed in the bath at 195° C.

Analysis:	Calc. for $C_{16}H_{17}N_2SI$:	C, 48.46;	H, 4.33
	Found:	C, 48.69;	H, 4.10

10. 2-Amino-5-dimethylaniline-thiosulfuric acid.

This compound was prepared according to the method described by Wahl.[17] Nineteen grams of freshly prepared p-nitrosodimethylaniline hydrochloride were dissolved in a mixture of 120 cc. of water and 40 g. of glacial acetic acid. This solution was cooled and a cold solution of 82 g. of $N_2S_2O_3 \cdot 5H_2O$ (10% excess) dissolved in 120 cc. of water was added. The temperature was kept below 5° C. and stirred for 2 hours. The mixture was then poured into a flask, stoppered and placed in an ice box for 48 hours. The thiosulfuric acid derivative was then filtered off and dried; yield 13 g. 50% of crude product. After several recrystallizations from water a sample was obtained in clear colorless crystals that gradually turned light blue. M.P. dec. 202-204° C. as previously reported.

11. 2(p-Nitrophenyl)-6-dimethylamino-benzothiazole.

Two and a half grams of 2-amino-5-dimethylaniline-thiosulfuric acid were suspended in 100 cc. of glacial acetic acid, heated to boiling and 2 g. of p-nitrobenzoylchloride were added and the solution kept boiling for an hour. The solution was then filtered hot and on cooling red crystals separated. The crystals were filtered off and the filtrate was poured into a liter of water. A red precipitate settled out which was filtered off and recrystallized; yield 1.5 g. of purified product, m.p. after one recrystallization 244-245° C. (corr.) as previously reported by Bogert and Updike.[29]

12. 2(p-Aminophenyl)-6-dimethylamino-benzothiazole.

This compound was prepared according to the method of Bogert and Updike.[29] Five grams of the crude nitro compound were suspended in 200 cc. of water and 20 cc. of conc. HCl, and 10 g. of tin were added. The mixture was boiled for 10 hours. After removing the excess tin the solution was poured into 4N. NaOH solution and boiled for an hour. After settling it was filtered and the free base was recrystallized from alcohol; yield 2.5 g. 57% after one recry. The m.p., 221° C. (corr.), agrees with that previously reported.

13. 2-Phenyl-6-dimethylamino-benzothiazole.

Five grams of 2-amino-5-dimethylaniline-thiosulfuric acid were dissolved in 50 cc. of water and a mixture of 50 cc. of methanol and 5 cc. of benzaldehyde was added. The mixture was kept on a steam plate for 4 hours. It was then allowed to cool, was filtered. The filtrate was diluted with water and kept on the steam plate for 6 hours. A second crop of crystals separated, which were filtered off and added to the first crop of crystals. The product was dissolved in methanol, norited and filtered. Two and three-tenth grams of yellow crystals were obtained. m.p. 134-135° C. (corr.). This agrees with the m.p. reported by Bogert and Updike.[29]

This compound was also prepared from 6-amino-2-phenylbenzothiazole according to the method described by Bogert and Abrahamson.[21] The results checked and a mixed melting point was unchanged.

14. Methylation of 2-phenyl-6-dimethylamino-benzothiazole.

Three grams of 2-phenyl-6-dimethylamino-benzothiazole and 5 cc. of methyl iodide were heated in a Parr bomb for 6 hours at 100-110° C. The excess methyl iodide was driven off and the residue extracted with hot water. Three and eight-tenth grams of crude product were obtained. After several recrystallizations from water it came down in long mica like crystals; m.p. 202-3°

C. (corr.) with dec. when placed in the bath at 195° C.

Analysis: Calc. for $C_{16}H_{17}N_2SI$: C, 48.46; H, 4.33
Found: C, 48.38; H, 4.47

15. 2(p-Dimethylaminophenyl)-6-dimethylamino-benzothiazole.

A. *The Anil.*

Ten grams of 2-amino-5-dimethylaniline-thiosulfuric acid were dissolved in 200 cc. of boiling water and a solution of 7 g. of p-dimethylamino-benzaldehyde dissolved in 50cc. of boiling alcohol was added. The solution turned red and in a few minutes the anil separated in glistening red needles; yield 12 g., about 78%. After several recrystallizations from alcohol, in which it is only slightly soluble, it melted with dec. at 210-215° C. as reported by Bogert and Updike.[29]

B. *Cyclization.*

Prolonged boiling of the anil in a large volume of acetic acid effected ring closure as reported by Bogert and Updike.[29] Much quicker results were obtained by boiling with aniline. Twelve grams of the anil were covered with 20 cc. of aniline and heated in an oil bath until the aniline boiled and kept at this temperature for about an hour. The mixture was filtered while hot and a white residue remained in the funnel. Aniline was boiled off until crystals began to form and then the solution was cooled slowly. Seven grams, about 81% of the crude yellow crystals were obtained. After several recrystallizations from acetic acid the m.p. 230-231° C. (corr.) checked with that previously reported.

16. Methylation of 2(p-dimethylaminophenyl)-6-dimethylamino-benzothiazole.

Three grams of 2(p-dimethylaminophenyl)-6-dimethylamino-benzothiazole and 5 g. of methyl iodide were heated in a Parr bomb for 12 hours at 100-110° C. The bomb was cooled, opened and the contents extracted with hot water, 2 g. of a yellow crystalline product were obtained, which after numerous recrystallizations melted at 224-5° C. (corr.) with dec. when placed in the bath at 220° C. Analysis checked for a mono methiodide. It is only moderately soluble in water but extremely soluble in methanol from which it crystallizes in fine orange red needles.

Analysis: Calc. for $C_{18}H_{22}N_3SI$: C, 49.19; H, 5.05.
Found: C, 49.26; H, 4.78.

The filtrate from the above extraction was evaporated almost to dryness and about 2 more g. of product were obtained. This product was much lighter in color and extremely soluble in water but only moderately soluble in alcohol, from which it was recrystallized several times; m.p. 203-4° C. (corr.) with dec. when placed in the bath at 195° C. Analysis checks for a dimethiodide.

Analysis: Calc. for $C_{19}H_{25}N_3SI_2$: C, 39.23; H, 4.34
Found C, 39.43; H, 4.56

17. 2(p-Iodotrimethylaminophenyl) - 6 - dimethylamino-benzothiazole.

One gram of 2-amino-5-dimethylaniline-thiosulfuric acid was dissolved in 100 cc. of water and a solution of 1.2 g. of the methiodide of p-dimethylamino benzaldehyde dissolved in 50 cc. of alcohol was added. The mixture was brought to a boil and then placed on a steam plate for an hour. As the solution cooled 1.1 g. of crude product separated, which after several recrystallizations from water melted at 210-211° C. (corr.) with dec. This compound is moderately soluble in menthanol from which it crystallizes in light brown curving blades.

Analysis: Calc. for $C_{18}H_{22}N_3SI$: C, 49.19; H, 5.05
Found: C, 49.40; H, 5.11

18. p-Phenylenediamine-thiosulfuric acid.

This compound was prepared by the method described by Bernthsen[15] with slight modifications. Three grams of p-phenylenediamine were dissolved in a mixture of 4 cc. of conc. HCl and 25 cc. of boiling water and to this hot solution 14.5 g. of powdered aluminium sulfate were added with constant stirring and the agitation was continued until the resulting paste was smooth. The mixture was then packed with ice and when cold, a cold solution of potassium dichromate and sodium thiosulfate-(12 g. of hypo and 3 g. of potassium dichromate were each dissolved in 15 cc. of boiling water, 25 g. of ice were added to the hot hypo solution and then the dichromate solution was added) —was added with rapid stirring and the agitation was continued for 15 minutes after all the solutions were together. The mixture was then filtered, transferred to flasks, stoppered and placed in an ice box for 48 hours. The product was then filtered off and recrystallized from hot water. When highly purified it crystallized in transparent crystals that turn light blue due to oxidation. The yield, about 60% of crude crystals, checks that reported by Bernthsen. Loss in weight when heated for an hour at 110° C. corresponds to one mole of water. Bernthsen did not mention any water of hydration for the monothio acid. M.P. 204-206° C. (corr.) with dec. No melting point was reported by previous investigators.

Analysis; Calc. for $C_6H_8O_3N_2S_2 \cdot H_2O$: S, 26.94
Found: S, 27.11

19. 2-Phenyl-6-amino-benzothiazole.

Ten grams of p-phenylenediamine-thiosulfuric acid were dissolved in 50 cc. of hot water, 50 cc. of alcohol were added, the solution was brought to a boil and a mixture of 50 cc. of alcohol and 10 cc. of benzaldehyde was added. The mixture was boiled for several hours, cooled and filtered. The precipitate was extracted with amyl alcohol until only a white insoluble powder was left. The white powder was dissolved in boiling HCl and the solution poured into excess ammonium hydroxide solution. The free amine thus obtained was extracted with alcohol; yield 2 g. about 22%. After several recrystallizations from alcohol and finally from ethyl acetate it melted sharply at 206-207° C. (corr.). A mixed melting point with the amino derivative prepared by the method described by Bogert and Abrahamson[21] was unchanged, proving that the two were identical.

The compound extracted by the amyl alcohol was recrystallized from amyl alcohol; yield 5 g. m.p. 166-167° C. After several recrystallizations from ethyl acetate it melted sharply at 168-169° C. (corr.). This compound has not yet been identified.

Analysis: Found: S, 10.21; C, 76.04; H, 5.10

Prolonged boiling in 40% sulfuric acid did not change the compound. Fusion with sulfur converted it into 2-2′-diphenylbenzobisthiazole; yield about 35%, m.p. 238-239° C. (corr.). A mixed m.p. with a sample of this compound prepared by the action of benzaldehyde on the dithiosulfuric acid derivative of p-phenylene-diamine was unchanged. The product is insoluble in 30% NaOH. Molecular weight, about 310.

20. 2(p-Nitrophenyl)-6(p-nitrobenzoylamino) benzothiazole.

Five grams of p-phenylenediamine-thiosulfuric acid were pulverized and suspended in 100 cc. of acetone and 7.5 g. of p-nitrobenzoyl-chloride were added. The mixture was shaken frequently for 8 hours and then allowed to stand for 10 hours. The light greenish gray of the thio acid was replaced by a yellow powder. The solid was filtered off and extracted with boiling nitrobenzene, from which it crystallized in fine orange needles. It was recrystallized several times from xylene in which it is very slightly soluble; yield of purified product .5 g. No melting or decomposition occurred below 300° C.

Analysis:	Calc. for $C_{20}H_{12}O_5N_4S$:	S, 7.63;
		C, 57.12;
		H, 2.88
	Found:	S, 7.06;
		C, 57.52;
		H, 3.10

21. 2(p-Nitrophenyl)-6-amino-benzothiazole.

Two grams of 2(p-nitrophenyl)-6(p-nitrobenzoylamino) benzothiazole were refluxed with 40% sulfuric acid until it completely dissolved. The solution was diluted and neutralized with 30% NaOH solution. The resulting precipitate was recrystallized several times from alcohol and finally from ethyl acetate from which it came down in beautiful deep red crystals; yield .7 g. of purified product; m.p. 266-270° C.

Analysis:	Calc. for $C_{13}H_9O_2N_3S$:	C, 57.53;	H, 3.35
	Found:	C. 57.57;	H, 3.37

22. 2(p-Aminophenyl)-6-amino-benzothiazole.

Four grams of crude 2(p-nitrophenyl)-6(p-nitrobenzoylamino) benzothiazole were suspended in 200 cc. of water and 20 cc. of conc. HCl. 10 g. of tin were added and the mixture was refluxed until the nitro derivative completely dissolved. The solution was then filtered into excess 30% NaOH and boiled for 30 minutes. The free amine was filtered off and recrystallized several times from alcohol; yield 0.6 g. about 50%. A highly purified sample melted 258-9° C. (corr.).

Analysis;	Calc. for $C_{13}H_{11}N_3S$:	C, 64.68
		H, 4.59
		S, 13.29
	Found:	C, 65.14
		H, 4.70
		S, 13.25

Reduction of 2(p-nitrophenyl)-6-amino-benzothiazole was carried out under similar conditions. A mixed melting point with the product obtained above was unchanged.

23. 2(p-Dimethylaminophenyl)-6-amino-benzothiazole.

A. *The Anil.*

Ten grams of p-phenylenediamine-thiosulfuric acid were dissolved in 200 cc. of boiling water and 50 cc. of alcohol added, and then a solution of 7.5 g. of p-dimethylamino-benzaldehyde dissolved in 50 cc. of alcohol was added. The solution immediately turned red, and in a few minutes a mass of fine red crystals formed. The mixture was kept warm for 30 minutes, cooled and filtered. 14 g. of crude product, about 90%, were obtained. It is very slightly soluble in alcohol from which it crystallizes in glistening red needles. It gradually softens around 240 and at about 270° C. decomposes rapidly.

Analysis:	Calc. for $C_{15}H_{17}O_3N_3S_2$:	S, 18.25
	Found:	S, 18.09

B. *Cyclization.*

Ten grams of the above anil were covered with 20 cc. of aniline and heated to boiling for 30 minutes and filtered while hot. When the filtrate cooled it was filtered and this filtrate was diluted with 50% alcohol and more of the desired product separated. About 2 g. of crude product were obtained. After several recrystallizations from alcohol and several from ethyl acetate it crystallized in fine almost white needles; m.p. 229-230° C. (corr.).

Analysis; Calc. for $C_{15}H_{15}N_3S$: C, 66.86; H, 5.62
Found: C, 66.75; H, 5.58

24. 2(p-Nitrophenyl)-6(p-nitrobenzalamino) benzothiazole.

Five grams of p-phenylenediamine-thiosulfuric acid were dissolved in 100 cc. of boiling water and a solution of 7.5 g. of p-nitrobenzaldehyde dissolved in 100 cc. of boiling alcohol was added. The solution turned red and in a few minutes fine red needles began to separate out. The mixture was kept on the steam plate for 30 minutes. cooled and filtered; yield 5 g. about 60% of crude product. After several recrystallizations from xylene it was obtained in fine red needles that melted 240-246° C. (corr.).

Analysis; Calc. for $C_{20}H_{12}O_4N_4S$: C, 59.38; H, 2.99
Found: C, 59.48; H, 3.13

Attempts to hydrolyze this compound with either conc. HCl or 40% sulfuric acid were unsuccessful.

Reduction with tin and HCl resulted in the formation of 6-amino - 2 - (p-aminophenyl) benzothiazole. A mixed melting point with a sample obtained in (22) was unaltered.

25. The action of p - iodotrimethylamino - benzaldehyde on p-phenylenediamine-thiosulfuric acid.

A solution of 1 g. of the thio acid dissolved in 50 cc. of boiling water was mixed with a solution of 1.5 g. of the above aldehyde dissolved in 50 cc. of boiling alcohol and the mixture was placed on a steam plate for an hour. The solution which was light orange red at first turned yellow and on cooling about a g. of white solid separated and was filtered and washed with alcohol. The filtrate was evaporated on the steam plate to about half the original volume and on cooling another g. of product was obtained. This product was recrystallized by suspending the solid in 100 cc. of boiling alcohol and hot water added until the solid just dissolved. This solution was light yellow with a decided greenish fluorescence, and as the solution cooled the product separated in almost white needles. Analysis indicates that two moles of the aldehyde reacted with one of the thio acid to form 2(p-iodotrimethylaminophenyl)-6(p-iodotrimethylminobenzalamino) benzothiazole; m.p. 187-8° C. (corr.) with dec. when placed in the bath at 180° C.

Analysis:	Calc. for $C_{26}H_{30}N_4SI_2$:	C, 46.55;	H, 4.51
	Found:	C, 46.20;	H, 4.99

26. p-Phenylenediamine-1-4-dithiosulfuric acid, potassium salt.

This compound was prepared by the method described by Green and Perkin[19] with a few modifications. The following solutions were prepared and cooled.

(A) Six grams of p-phenylenediamine were dissolved in a mixture of 25 cc. of water and 27 g. of glacial acetic acid. (B) Thirteen and three-tenth grams of potassium dichromate were dissolved in 25 cc. of water and 6 g. of potassium carbonate were added. The mixture was heated until all the solid had dissolved and then allowed to cool. (C) Fifty grams of sodium thiosulfate crystals were dissolved in 25 cc. of boiling water. When crystals began to form in (B) 50 g. of ice were added and then (B) and (C) were mixed and this mixture was added in a steady stream to (A) to which 30 g. of fine ice had been added. The mixture was stirred during the mixing and continued for an hour, 50 g. of KCl were added and the stirring continued for another hour and filtered. The dithio acid was recrystallized from hot water and salted out with KCl. The yield checked those reported by Green and Perkin.[19]

A sample of the free dithio acid was obtained by adding conc. HCl to a saturated solution of the potassium salt. The product after several crystallizations was obtained in clear straw yellow crystals as previously reported.

27. 2-2′ Diphenyl-benzobisthiazole.

This compound was prepared by the method described by Green and Perkin.[19] Four grams of the potassium salt of the dithio acid were dissolved in 50 cc. of water, 3 cc. of conc. HCl and a mixture of 5 cc. of benzaldehyde and 50 cc. of alcohol was added. The mixture was heated for an hour on the steam plate, cooled and filtered. The crude product was recrystallized several times from glacial acetic acid and then from ethyl acetate from which it crystallized in pure white fine needles; m.p. 237-8° C. Green and Perkin reported a m.p. of 233-235° C.

28. 2-2′-Di(p-dimethylaminophenyl) benzobisthiazole.

A. *The Anil.*

Ten grams of the potassium salt of the dithio acid were dissolved in 100 cc. of boiling water, acidified with 5 cc. of conc. HCl and a solution of 8 g. of p-dimethylamino-benzaldehyde dissolved in 50 cc. of boiling alcohol was added. The solution turned red and in a few minutes a fine red precipitate settled out of the solution. The mixture was kept on a steam plate for 30 minutes, cooled and filtered. The anil is very slightly soluble in methanol from which it was recrystallized. It has no melting point but gradually turns brown and softens above 200° C. Analysis does not check for the bis anil type expected but checks for the p - dimethylamino - benzal derivative of 2(p - dimethylamino-phenyl) - 6 - amino - benzothiazole- 5 -thiosulffuric acid. Eleven grams of crude product were obtained about 90%. The filtrate was boiled with dilute nitric acid and barium chloride was added. Five and a half grams of barium sulfate were obtained. This is about 97% of the weight of barium sulfate that could have been formed if cyclization occurred on one side.

Analysis; Calc. for $C_{24}H_{24}O_3N_4S_3$: S, 18.77
Found: S, 18.35

B. *Cyclization.*

Ten grams of the anil were boiled with 30 cc. of aniline for an hour and filtered. As the filtrate cooled about 5 g. of crude product crystallized. It is very soluble in hot aniline, moderately soluble in xylene and slightly soluble in amyl alcohol and in ethyl acetate; m.p. 297° C. (corr.).

Analysis; Calc. for $C_{24}H_{22}N_4S_2$: C, 66.93; H, 5.15
Found: C, 67.00; H, 5.10

29. Attempts to prepare methiodides of 2-2′-di(p-dimethylaminophenyl) benzobisthiazole.

All attempts, to prepare methiodides either by the action of methyliodide on the above bisthiazole or by the action of the methiodide of p-dimethylaminobenzaldehyde on the dithio acid of p-phenylenediamine, failed.

30. Methiodide of p-dimethylamino-benzaldehyde.

Ten grams of p-dimethylamino-benzaldehyde and 7 cc. of methyl iodide were sealed in a Parr bomb and heated for 6 hours at 90-100° C. The bomb was cooled, opened and the contents were washed in boiling ethyl acetate to remove any unchanged p-dimethylamino-benzaldehyde. Nineteen grams of a white crystalline product were obtained. Fifteen grams of product melting 151-2° C. were obtained after one recrystallization from alcohol. Hodgson and Cooper reported a m.p. of 151-2. When a purified sample is placed in the bath at 150° C. sharp dec. takes place at 154-5° C. (corr.).

31. Dye Tests.

All the dye tests on the methiodides prepared in the investigation were carried out according to the method described by Bogert and Allen.

1 g. of pure white silk.
20 cc. of 0.1% dye solution (0.02 g. of dye).
25 cc. of water.
10 cc. of 2% neutral soap solution.
5 cc. of 2% salt solution.

The silk was boiled in a 10% neutral soap solution, rinsed and placed in the warm dye solution. The dye bath was gradually heated to boiling and allowed to simmer for 30 minutes.

BIBLIOGRAPHY

[1] 1870 Merz & Weith, Ber. **3,** 978.

[2] 1871 Merz & Weith, Ber. **4,** 393.

[3] 1881 Hess, Ber. **14,** 488.

[4] 1885 D. R. P. **35,** 790, Friedlander **1,** 535.

[5] 1888 Green, J. Soc. Chem. Ind., 1888. VII, 179.

[6] 1888 Brit. Pat., 6319.

[7] 1889 Green, J. Chem. Soc. **55,** 227.

[8] 1889 Green, Ber. **22,** 969.

[9] 1889 Rosenheck, U. S. Pat. **412,** 978.

[10] 1889 Rosenheck, U. S. Pat. **412,** 979.

[11] 1889 Jacobson, Ber. **22,** 330.

[12] 1889 Gattermann, Ber. **22,** 422.

[13] 1889 Gattermann, Ber. **22,** 425.

[14] 1889 Pfitzinger & Gattermann, Ber. **22,** 1064.

[15] 1889 Bernthsen, Ann. **251,** 1-97.

[16] 1892 Gattermann & Neuberg, Ber. **25,** 1082.

[17] 1901 Walh, Compt. rendu. **133,** 1216.

[18] 1902 Wohlfahrt, J. prakt. Chem. **2-66,** 553.

[19] 1903 Green and Perkin, J. Chem. Soc. 83, 1201.

[20] 1920 Möhlau & Bucherer. Farbenchemisches Praktikum, 271.

[21] 1922 Bogert & Abrahamson, J. Am. Chem. Soc. **44,** 826.

[22] 1923 Schultz, Farbstoff Tabellen, No. 618.

[23] 1923 Cain & Thorpe, The Synthetic Dyestuffs & Intermediate Products.

[24] 1923 Mills, Clark & Aeschlimann, J. Chem. Soc. **123,** 2353.

[25] 1924 Bogert & Snell, J. Am. Chem. Soc. **46,** 1308.

[26] 1924 Heller, Quast & Blanc, J. prakt. Chem. (2) **108,** 257.

[27] 1925 Clark, J. Chem. Soc. **127,** 973.

[28] 1926 Bogert & Corbitt, J. Am. Chem. Soc. **48,** 784.

[29] 1926 Bogert & Allen, J. Am. Chem. Soc. **49,** 1315.

[30] 1927 Bogert & Updike, J. Am. Chem. Soc. **49,** 1373.

[31] 1929 Hodgson and Cooper, J. Chem. Soc. 1929, 233.

[32] 1931 Bogert & Sevag, J. Am. Chem. Soc. **53,** 660.

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